# Moderna Completes Enrollment of Cytomegalovirus (CMV) Vaccine (mRNA-1647) Phase 2 Study

March 3, 2020

*Phase 2 interim data at three months, expected in 3Q 2020, intended to inform Phase 3 dose selection*

*Pivotal Phase 3 study manufacturing and planning underway; study start expected in 2021*

*CMV is the most common infectious cause of birth defects in the U.S.; there is no approved vaccine to prevent CMV*

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Moderna, Inc., (Nasdaq: MRNA) a clinical stage biotechnology company pioneering messenger RNA (mRNA) therapeutics and vaccines to create a new generation of transformative medicines for patients, today announced that enrollment is complete for all three dose cohorts of the Phase 2 dose-confirmation study of its investigational cytomegalovirus (CMV) vaccine (mRNA-1647). mRNA-1647, the first mRNA vaccine for an infectious disease to enter a Phase 2 study, is a wholly owned program in Moderna's prophylactic vaccines portfolio.

On January 9, the Company announced positive seven-month interim safety and immunogenicity data after the third and final vaccination of the 30, 90, and 180 µg dose level cohorts of the Phase 1 study, which built on the previously reported three-month interim analysis, after two vaccinations. The first interim analysis of the Phase 2 study is expected in the third quarter of 2020.

"I would like to thank the dedicated Moderna CMV team and our partners at clinical trial sites for their support in completing enrollment of the Phase 2 study ahead of plan," said Stéphane Bancel, Moderna's Chief Executive Officer. "We recognize the urgent need for a preventative vaccine against CMV in women of childbearing age, which we believe positions our wholly owned mRNA-1647 program as a potential blockbuster commercial and clinical opportunity. We believe our CMV vaccine will build Moderna's future and embodies our mission of creating a new generation of transformative medicines for patients. The Moderna team is working diligently to start the Phase 3 study in 2021."

The Phase 2 study is evaluating the safety and immunogenicity of mRNA-1647 in 252 healthy adults in the U.S. at three dose levels (50, 100 and 150 µg) in both CMV-seronegative and CMV-seropositive participants administered in a three-dose vaccination schedule (0, 2 and 6 months). The first interim analysis at three months (one month after the second vaccination) is expected in the third quarter of 2020 and is intended to inform Phase 3 dose selection. The Company is actively preparing for a Phase 3 pivotal study expected to start in 2021, which will evaluate prevention of primary CMV infection in a population that includes women of childbearing age.

mRNA-1647 comprises six mRNAs encoding two antigens in one vaccine and is designed to protect against CMV infection. Of the six mRNAs, five encode the subunits of the CMV pentamer complex and one mRNA encodes the glycoprotein B (gB) protein, both of which are highly immunogenic. Both pentamer and gB proteins are essential for CMV to enter epithelial cells, which is the first step in CMV infection. mRNA-1647 is designed to produce an immune response to both pentamer and gB antigens to prevent CMV infection. There is no approved vaccine for CMV.

**About the Planned Phase 3 Study**

The Company is actively preparing for a global randomized, observer-blind, placebo-controlled Phase 3 pivotal study to evaluate the efficacy of mRNA-1647 against primary CMV infection. Moderna has solicited and received Type C meeting feedback from the FDA on the preliminary design of the pivotal trial, which will evaluate prevention of primary CMV infection in a population that includes women of childbearing age. The Company believes this can be achieved with a trial with no more than 8,000 participants and feasibility assessments of study sites has already begun across North America and Europe. After the Phase 2 three-month data are analyzed, which is expected in the third quarter of 2020, these data will inform the dose selection for the Phase 3 pivotal study. The pivotal trial design will be finalized after discussion with the FDA and other global health authorities. Manufacturing and planning are already underway for this pivotal study, which is expected to start in 2021.

**About mRNA-1647**

mRNA-1647 comprises six mRNAs encoding two antigens in one vaccine and is designed to protect against CMV infection. Of the six mRNAs, five encode the subunits of the CMV pentamer complex and one mRNA encodes the glycoprotein B (gB) protein, both of which are highly immunogenic. The pentamer complex is important for CMV entry into a variety of cells, including epithelial cells, while gB is important for entry into all susceptible cells including fibroblasts. A vaccine that produces an immune response against both pentamer and gB has the potential to prevent CMV entry into a range of target cell types and thus prevent primary and congenital infections. Unlike a protein-based vaccine, mRNA-1647 instructs the body's own cells to manufacture the antigens, resulting in functional antigens that mimic those presented to the immune system by CMV during a natural infection. Preclinical data previously published in *Vaccine* showed that vaccination with mRNA-1647 in animal models elicited potent and durable neutralizing antibody titers.

**About Cytomegalovirus (CMV)**

CMV is a common pathogen and member of the herpesvirus family. Congenital (present at or before birth) CMV infection results when infected mothers transmit the virus to their unborn child, and it is the leading infectious cause of birth defects in the United States with approximately 25,000 newborns in the U.S. infected every year.[1,2] Approximately 20 percent of infected infants will have birth defects that include neurodevelopmental disabilities such as hearing loss, vision impairment, varying degrees of learning disability and decreased muscle strength and coordination.[3] There is currently no approved vaccine for the prevention of CMV infection.

CMV infection is common in young children who have never been exposed to the virus, and is acquired and spread through contact with saliva, breastmilk, mucus and urine. As a result, young children can be a major source of infection for pregnant women, particularly mothers, daycare workers, preschool teachers, therapists and nurses. Efforts to create a vaccine began in the 1970s, and in 1999 the Institute of Medicine (now National Academy of Medicine) designated CMV as a "highest priority" category for vaccine development. Prior studies of investigational vaccines that did not protect against the CMV pentamer antigen demonstrated limited efficacy against CMV infection and limited durability of immune response.

**About Moderna's Core Prophylactic Vaccines Modality**

Moderna scientists designed the Company's prophylactic vaccines modality to prevent infectious diseases. More than 1,400 participants have been enrolled in Moderna's infectious disease vaccine clinical studies under health authorities in the U.S., Europe and Australia. Based on clinical experience across six Phase 1 studies, the Company has designated prophylactic vaccines a core modality and intends to accelerate development of its infectious disease vaccine candidates.

The potential advantages of an mRNA approach to prophylactic vaccines include the ability to mimic natural infection to stimulate a more potent immune response, combining multiple mRNAs into a single vaccine, rapid discovery to respond to emerging pandemic threats and manufacturing agility derived from the platform nature of mRNA vaccine design and production. Moderna has built a fully integrated manufacturing plant in Norwood, MA which enables the promise of the technology platform.

Moderna currently has nine development candidates in its prophylactic vaccines modality, including:

*Vaccines against respiratory infections*

- Respiratory syncytial virus (RSV) vaccine for older adults (mRNA-1777 and mRNA-1172 or V172 with Merck)
- RSV vaccine for young children (mRNA-1345)
- Human metapneumovirus and parainfluenza virus type 3 (hMPV/PIV3) vaccine (mRNA-1653)
- Novel coronavirus (SARS-CoV-2) vaccine (mRNA-1273)
- Influenza H7N9 (mRNA-1851)

*Vaccines against infections transmitted from mother to baby*

- Cytomegalovirus (CMV) vaccine (mRNA-1647)
- Zika vaccine (mRNA-1893) with the Biomedical Advanced Research and Development Authority (BARDA)

*Vaccines against highly prevalent viral infections*

- Epstein-Barr virus (EBV) vaccine (mRNA-1189)

To date, Moderna has demonstrated positive Phase 1 data readouts for six prophylactic vaccines (H10N8, H7N9, RSV, chikungunya virus, hMPV/PIV3 and CMV). Moderna's CMV vaccine is currently in a Phase 2 dose-confirmation study. Moderna's investigational Zika vaccine (mRNA-1893), currently in a Phase 1 study, was granted FDA Fast Track designation.

**About Moderna**

Moderna is advancing messenger RNA (mRNA) science to create a new class of transformative medicines for patients. mRNA medicines are designed to direct the body's cells to produce intracellular, membrane or secreted proteins that can have a therapeutic or preventive benefit and have the potential to address a broad spectrum of diseases. Moderna's platform builds on continuous advances in basic and applied mRNA science, delivery technology and manufacturing, providing the Company the capability to pursue in parallel a robust pipeline of new development candidates. Moderna is developing therapeutics and vaccines for infectious diseases, immuno-oncology, rare diseases, cardiovascular diseases, and autoimmune and inflammatory diseases, independently and with strategic collaborators. Moderna has 24 mRNA development candidates in its portfolio across all modalities, with 12 in clinical studies. Four of these programs are in or preparing for Phase 2 studies and the Company is preparing for its first Phase 3 study.

Headquartered in Cambridge, Mass., Moderna currently has strategic alliances for development programs with AstraZeneca, Plc. (Nasdaq: AZN) and Merck, Inc. (Nasdaq: MRK), as well as the Defense Advanced Research Projects Agency (DARPA), an agency of the U.S. Department of Defense; the Biomedical Advanced Research and Development Authority (BARDA), a division of the Office of the Assistant Secretary for Preparedness and Response (ASPR) within the U.S. Department of Health and Human Services (HHS). Moderna has been named a top biopharmaceutical employer by *Science* for the past five years. To learn more, visit www.modernatx.com.

**Forward Looking Statements**

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended including, the ongoing planning for a pivotal Phase 3 study for mRNA-1647; the expected timing of data from the Phase 2 trial; the scope and size of the Phase 3 trial; the potential size of the market for a CMV vaccine and the Company's belief that it can reduce the burden of CMV infection, including in women of childbearing age. In some cases, forward-looking statements can be identified by terminology such as "will," "may," "should," "expects," "intends," "plans," "aims," "anticipates," "believes," "estimates," "predicts," "potential," "continue," or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. The forward-looking statements in this press release are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond Moderna's control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. These risks, uncertainties, and other factors include, among others: the actual results of the Phase 2 study; the finalization of the Phase 3 trial design and implementation activities; the fact that there has never been an approved mRNA based vaccine or therapeutic approved for human use and those other risks and uncertainties described under the heading "Risk Factors" in Moderna's most recent Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission (SEC) and in subsequent filings made by Moderna with the SEC, which are available on the SEC's website at www.sec.gov. Except as required by law, Moderna disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press release in the event of new information, future developments or otherwise. These forward-looking statements are based on Moderna's current expectations and speak only as of the date hereof.

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[1] Congenital CMV and Hearing Loss. Centers for Disease Control and Prevention. Available at https://www.cdc.gov/cmv/hearing-loss.html.

[2] Schleiss et al. Progress toward development of a vaccine against congenital cytomegalovirus infection. *Clinical and Vaccine Immunology*. 2017;

24(12): e00268-17.
[3] Congenital CMV and Birth Defects. American Pregnancy Association. Available at: https://americanpregnancy.org/birth-defects/congenital-cmv-birth-defects/.

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